

EDITORIAL

TWO DECADES IN THE SUN: THE WELCOME-MAHIDOL-OXFORD VENTURE

Southeast Asia has been host to many international adventurers in science this century and before. It was, for example, the observation mid last century of the dramatic differences between bird and plant species on Bali and on Lombok - neighboring Indonesian islands just 24 kilometers apart - that led Alfred Russell Wallace to his critical contribution to the most revolutionary theory in the whole of biology: the theory of evolution of species. It was that observation that inspired him to write to Charles Darwin, shattering Darwin's solace, raising in him the fear that his unpublished work of twenty years might be scooped by this young adventurer working in the distant field. This dilemma was transiently resolved by their publication of a joint paper carrying the first open announcement to the world. This paper came to lie in the shadow of *The Origin of Species* but in the objective history of evolution theory it was the first public record. Wallace may arguably have had reason to resent the asymmetric shadow that eventually was cast as the world tended to forget his effort and referred to *Darwinian theory*, but nothing detracts from his brilliant interpretation of the wealth of information that was to be gained from the natural history of this prolific region. The *Wallace Line* that runs between Bali and Lombok is perhaps a fitting reminder of the global importance of his work even beyond biology in the clues it provided to the later theory of plate tectonics in the formation of the continents. Indirectly in this sense perhaps Wallace survived his eclipse by Darwin.

The wealth of information to be found in the natural history of Southeast Asia has also made critical contributions to tropical medicine, not least in the past few decades, for natural history is the very grass roots essence of this field. In the shadow of the prodigious explosion of molecular biology and immunology the fundamental contribution made by observational natural history in the field and at the bedside is often deprived of just recognition. Much of the progress in communicable disease control lies in delineating the subtleties of interaction between infectious agent and host in the context of physical environment. There is a rich literature attesting to the contributions of this type that have been made

by medical scientists in the countries of this region over a long period to the definitive natural history of tropical infectious diseases like malaria, filariasis, dengue, hepatitis, leprosy, enteric infections, melioidosis, fluke-induced hepatic disease and many others. They have used this basis to advantage in descriptive and quantitative epidemiological analysis and in the application of the tools of molecular science to selection of improved therapeutic options. It is a rich recent addition to a long history.

This history is also full of productive international collaborations of many different kinds, with investigators from many nations: ASEAN countries, United States, Japan, Germany, France, Canada and many others. This internationalization has contributed technology, training, funds, ideas, perspective and mutual recognition. It has engendered a global view and has set the scene now for an increasing regional input to the solutions to many pressing problems of tropical medicine. Most importantly it has enabled creative younger generations to invest their lives in science with a clear purpose to tackle the tough issues of more effective disease prevention and control in the Southeast Asian cauldron. For cauldron it surely is, as attested by its inadvertent role as the global epicenter of multi-drug resistant malaria, as the epitome of rapid inter-country spread of HIV/AIDS associated with the inexorable mobility of populations, as the extraordinary world focal point of parasite-related cholangiocarcinoma and many other intriguing dramas.

In this context it is of special interest to read in this journal issue the account by Nick White of the Wellcome-Mahidol-Oxford experiment of on-site collaboration in Thailand and beyond on the occasion of its twenty year celebration. This paper traces with great clarity the detailed evolutionary journey of people, projects and propositions. It is a fascinating story that rightly acknowledges the far-sighted pragmatism of the Dean-extraordinaire of Mahidol University's Faculty of Tropical Medicine, Prof Chamlong Harinasuta, and the UK's resource-rich, innovative Wellcome Trust. It should be remembered that for nearly twenty years before this venture was discussed this Faculty under Prof Chamlong's leadership had become the coordinating center of

regional training and research in the field of tropical infectious disease, so that it was in a position of considerable strength in intrinsically driven experience, even though it depended heavily on international sources of funding for its research programs.

Against this background the two partners in that venture no doubt each brought pride to the partnership, even though it may have been expressed in different ways reflecting their cultural differences, the British with a certain haughtiness and perhaps a neo-colonial sense of mission, the Thai with outward, deceiving humility and inner certainty. These differences required a willingness on both sides to follow a mutual learning curve. The laboratory kindly provided by the Faculty was in truth the hospital's only clinical lab and, given the limited space at that time, the transition was not altogether easy for the hospital staff, but underlying emotions are so often suppressed in the Thai way and apparent acquiescence taken at face value by the west. By the same token the furrowed brow of the English is perhaps misinterpreted as arrogance when it simply reflects reserved self discipline. Sharing facilities long term like this is not always an easy compromise but it came to work well.

Malaria and snake bite made a productive combination as an opening gambit. The first was a field in which the Faculty of Tropical Medicine had already established a world reputation for clinical management and the epidemiology of drug resistance. The second was rather far from focal interests at that time. It was an appropriate mix and over the next several years important contributions to both fields emanated from the group that gathered together under the collaborative venture.

It so turned out that these past 20 years saw the gathering pace of genesis of drug resistant falciparum malaria in this region, creating an urgent need to find and try out many new anti-malarials. The Hospital for Tropical Diseases at the Faculty presented an appropriate milieu for clinical trials, leading on to field trials in rural areas. In a sense the impending disaster of multi-drug resistance provided a two-pronged opportunity. The hospital program was predominantly a Mahidol affair, while the field trials were a special challenge for the joint venture, involving a close partnership with the Malaria Division of the Ministry of Public Health that continues to this day. This complimentary requirement gave stimulus to fill a globally important niche in clinical malaria research: it may well be argued that accepting this challenge proved to be the making of major success for the venture. New drugs were im-

perative and what better place to test them out than in the global epicenter of resistance.

At the same time the Wellcome unit put a dedicated effort into providing a much improved definition of the pathophysiology of severe and cerebral malaria, leading to a compendium of systematic knowledge of importance for improving clinical management and reducing mortality. The very positive reputation of the Hospital for Tropical Diseases in the countryside led to large numbers of patient referrals and to the opportunity to apply this academic knowledge to the real world of patient survival or not. The new basic knowledge fed the action at the bedside and the patient data gave feedback to the laboratory and the field. The outcome was a database of quality and a well-developed capacity to undertake malaria drug trials of definitive world class. In the halls of power at WHO in Geneva in the early 1980s, however, western dominated committees lauded the Wellcome inputs but often tended to ignore the Thai contribution or consider it subservient: a nostalgic throw back to colonial times perhaps, important in a negative sense because research grants from that source depended on trust and respect.

A new boost of hope to the malarial world arrived in the form of a Chinese drug dating from 2000 years ago, qinghaosu. Synthetic derivatives were made in China and subjected to rigorous trials at the Hospital for Tropical Diseases. From the present perspective the positive outcome of the trials gave hope because of the different pharmacokinetics of this group of drugs to earlier ones. Combination therapy also came of age in the 1990s and is the hope for the immediate future. Has China received adequate kudos for these developments from Thailand or the world? That perhaps is an issue for historians to decide in the future but WHO bureaucratic diplomacy in the 1980s was not impressive and left the Chinese drug developers with little respect for western objectivity in the politics of science. Nevertheless the advent of these effective drugs, old in China but newly available to the world, gives now at least a breathing period in what is still a threatening scenario: will we run out of effective anti-malarials? The Wellcome-Mahidol-Oxford joint venture is at the forefront of this debate and a great deal rides on their work.

Diversification of the program to include studies on melioidosis in northeastern Thailand involved long term collaboration with Sappasitprasong Hospital in Ubon Ratchathani in epidemiology, diagnostic procedures and clinical management and led

to a substantial decrease in mortality. Other challenges have also been taken up from time to time but malaria remains the primary focus, justifiably, and the geographic spread of activities have wisely ventured beyond Thailand to other countries in the region. This focus has led to excellence and to major global contributions. In this sense the joint venture over 20 years has been a very positive model of what can be achieved by this type of international collaboration.

At the same time it is useful to reflect a little more deeply on what is appropriate and what might be done better in future or by other partners in similar ventures in other countries. The original agreement made provision of transition from British to Thai leadership within the first 10 years, yet as the second decade closes there is no evidence of that tran-

sition occurring, despite the issue having been raised critically at various times at high levels of Thai academe. Reminiscent perhaps of the competition for recognition in the arena of evolution theory over a century before? This is disappointing and outwardly tends to suggest Thai subservience, strangely perhaps in view of the proud international record of Thai medical science in many fields and in many institutions throughout the country during these recent decades. Shadows exclude the sun but eventually the sun warms even the shade. The ultimate success of collaborative ventures of this kind is enshrined in transition to true equality of recognition and leadership. The Wellcome-Mahidol-Oxford venture has achieved a great deal in its first 20 years: we look forward enthusiastically to a bright, equitable future.

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